

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
20 September 2001 (20.09.2001)

PCT

(10) International Publication Number
WO 01/68836 A3

(51) International Patent Classification⁷: **C12N 15/11**,
15/63, C12Q 1/68, A61K 31/7105

Road, Huntington, NY 11743 (US). **HANNON, Gregory**
[US/US]; 92 Sammis Street, Huntington, NY 11743 (US).

(21) International Application Number: PCT/US01/08435

(74) Agents: **VINCENT, Matthew, P.** et al.; Ropes & Gray,
One International Place, Boston, MA 02110 (US).

(22) International Filing Date: 16 March 2001 (16.03.2001)

(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(25) Filing Language: English

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(26) Publication Language: English

Published:

— with international search report

(30) Priority Data:

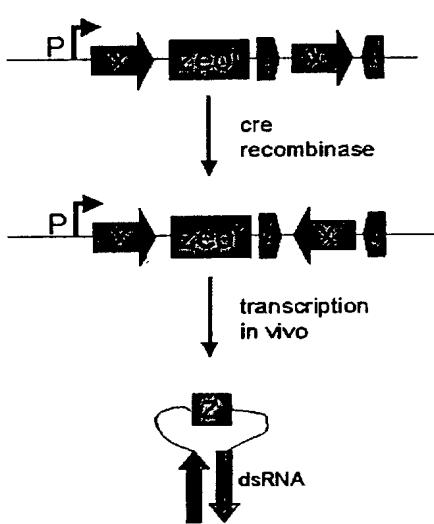
60/189,739 16 March 2000 (16.03.2000) US
60/243,097 24 October 2000 (24.10.2000) US

(71) Applicants (for all designated States except US): **GENETICA, INC.** [US/US]; Building 600, One Kendall Square, Cambridge, MA 02139 (US). **COLD SPRING HARBOR LABORATORY** [US/US]; One Bungtown Road, Cold Spring Harbor, NY 11724 (US).

(88) Date of publication of the international search report:
14 March 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND COMPOSITIONS FOR RNA INTERFERENCE



(57) Abstract: The present invention provides methods for attenuating gene expression in a cell using gene-targeted double stranded RNA (dsRNA). The dsRNA contains a nucleotide sequence that hybridizes under physiologic conditions of the cell to the nucleotide sequence of at least a portion of the gene to be inhibited (the "target" gene).

WO 01/68836 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/08435

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C12N15/63 C12Q1/68 A61K31/7105

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, CAB Data, SEQUENCE SEARCH, BIOSIS, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TUSCHL THOMAS ET AL: "Targeted mRNA degradation by double-stranded RNA in vitro." GENES & DEVELOPMENT, vol. 13, no. 24, 15 December 1999 (1999-12-15), pages 3191-3197, XP002183118 ISSN: 0890-9369 the whole document</p> <p>---</p>	1,9, 12-15
A	<p>WO 99 32619 A (CARNEGIE INST OF WASHINGTON ;MONTGOMERY MARY K (US); FIRE ANDREW () 1 July 1999 (1999-07-01) the whole document</p> <p>---</p> <p>---</p>	-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

16 November 2001

Date of mailing of the international search report

21/12/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Hornig, H

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/08435

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 29058 A (CARNEGIE INST OF WASHINGTON ;UNIV MASSACHUSETTS (US)) 26 April 2001 (2001-04-26) claims 1-16 ---	1-5, 9, 12-15
P, X	WO 00 44914 A (FARRELL MICHAEL J ;LI YIN XIONG (US); KIRBY MARGARET L (US); MEDIC) 3 August 2000 (2000-08-03) claims 1-61 ---	1, 9, 12-15
P, X	BERNSTEIN EMILY ET AL: "Role for a bidentate ribonuclease in the initiation step of RNA interference." NATURE (LONDON), vol. 409, no. 6818, 18 January 2001 (2001-01-18), pages 363-366, XP002183119 ISSN: 0028-0836 the whole document ---	1-15
T	HAMMOND SCOTT M ET AL: "Argonaute2, a link between genetic and biochemical analyses of RNAi." SCIENCE (WASHINGTON D C), vol. 293, no. 5532, 2001, pages 1146-1150, XP002183120 ISSN: 0036-8075 figure 3 ---	
T	MOSS ERIC G: "RNA interference: It's a small RNA world." CURRENT BIOLOGY, vol. 11, no. 19, 2001, pages R772-R775, XP002183121 ISSN: 0960-9822 page R773, right-hand column, line 8 -page R774, right-hand column, line 23 ---	
T	AMBROS VICTOR: "Dicing up RNAs." SCIENCE (WASHINGTON D C), vol. 293, no. 5531, 3 August 2001 (2001-08-03), pages 811-813, XP002183122 ISSN: 0036-8075 the whole document ---	
		-/-

INTERNATIONAL SEARCH REPORT

Int'l Application No

PCT/US 01/08435

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	CAPLEN N J ET AL: "dsRNA-mediated gene silencing in cultured Drosophila cells: a tissue culture model for the analysis of RNA interference" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 252, no. 1-2, 11 July 2000 (2000-07-11), pages 95-105, XP004210158 ISSN: 0378-1119 the whole document -----	1,9, 12-15
P,A	HAMMOND SCOTT M ET AL: "An RNA-directed nuclease mediates post-transcriptional gene silencing in Drosophila cells." NATURE (LONDON), vol. 404, no. 6775, 16 March 2000 (2000-03-16), pages 293-296, XP002183123 ISSN: 0028-0836 the whole document -----	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims (2,4-15)-partially (and as far as in vivo methods are concerned) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Although claims 18 and 19 could be, at least be partially be considered as scheme, rule and method for doing business, Rule 39.1(iii) PCT, the search has been carried out as far as possible in our systematic documentation.

Continuation of Box I.2

Claims Nos.: 17

Present claim 17 relate to a method of formulating a pharmaceutical preparation including one or more agents identified by an assay, without giving a true technical characterization. Moreover no such compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l Application No

PCT/US 01/08435

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9932619	A 01-07-1999	AU 1938099	A 12-07-1999	EP 1042462	A1 11-10-2000
		WO 9932619	A1 01-07-1999		
WO 0129058	A 26-04-2001	AU 1086501	A 30-04-2001	WO 0129058	A1 26-04-2001
WO 0044914	A 03-08-2000	AU 2634800	A 18-08-2000	EP 1147204	A1 24-10-2001
		WO 0044914	A1 03-08-2000		